FDA Safety Update Adverse Event Reporting: Clinical Investigator Responsibilities

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Outline

- IND new safety reporting requirements
- Reasons for the new requirements
- The language of reporting
- Today → Investigators responsibilities

  What & When to report

  Expedited vs. routine reporting

  IRB reporting
- RDRC safety reporting

IND-Overview of New Requirements: CFR 312.64

- The final rule, published September 2010
  - **Codifies FDA's expectations for timely review, evaluation, and submission of important and useful safety information**
  - **More fully defines responsibilities of sponsors and investigators (specifically submission of serious and unexpected suspected adverse reactions)**
- Implements internationally harmonized definitions and reporting standards to the extent possible
  - Clarifies confusing terminology in existing regulations
- Improves the utility of premarket safety reports, thereby enhancing human subject protection

- Reducing the number of uninformative reports will enhance the ability of sponsors, FDA, investigators, and IRBs to focus on safety issues that affect human subjects

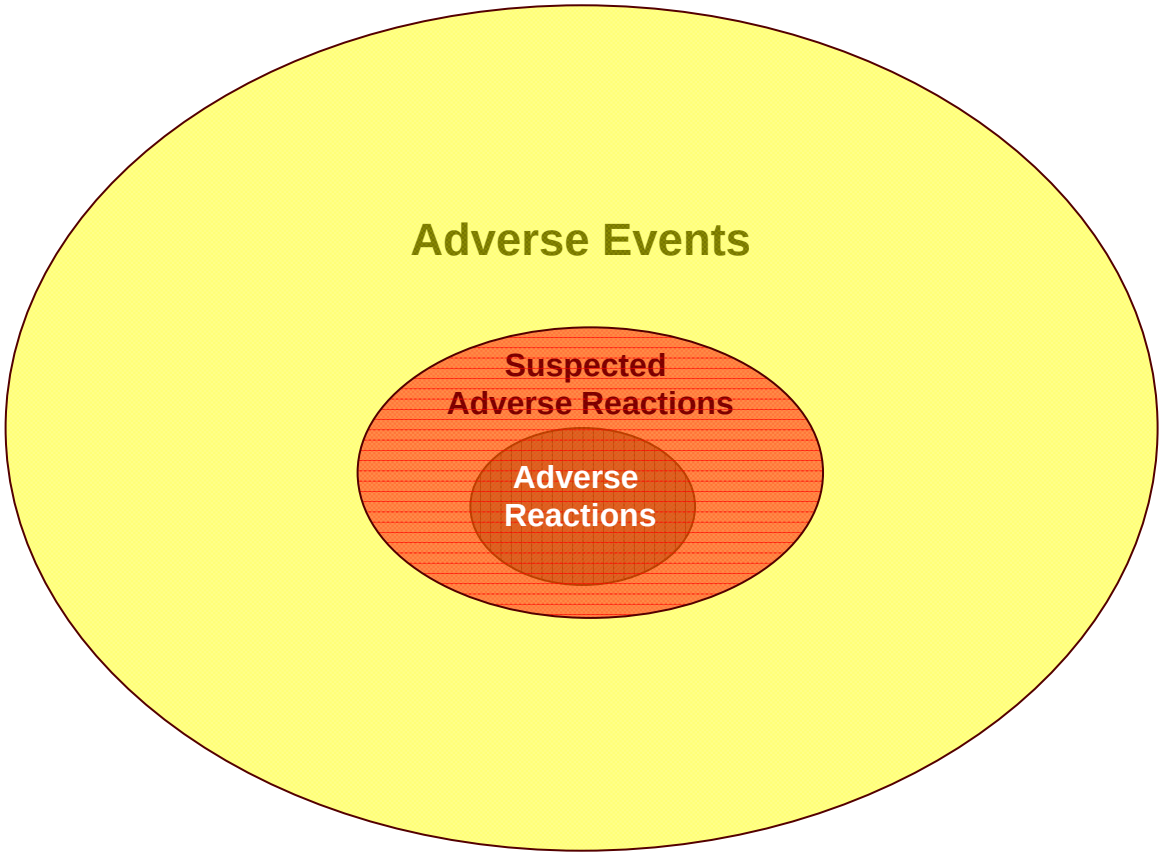
Lexicon

- What?
  - Adverse Event
  - Adverse Reaction
  - Factors – Serious, Expected, Causality
- When?
  - Expedited vs. Per Protocol

Adverse Event vs. Adverse Reaction

- Adverse Event -Any untoward medical occurrence associated with the use of a drug, *whether or not considered drug related*
- Adverse Reaction – Any Adverse Event caused by a drug

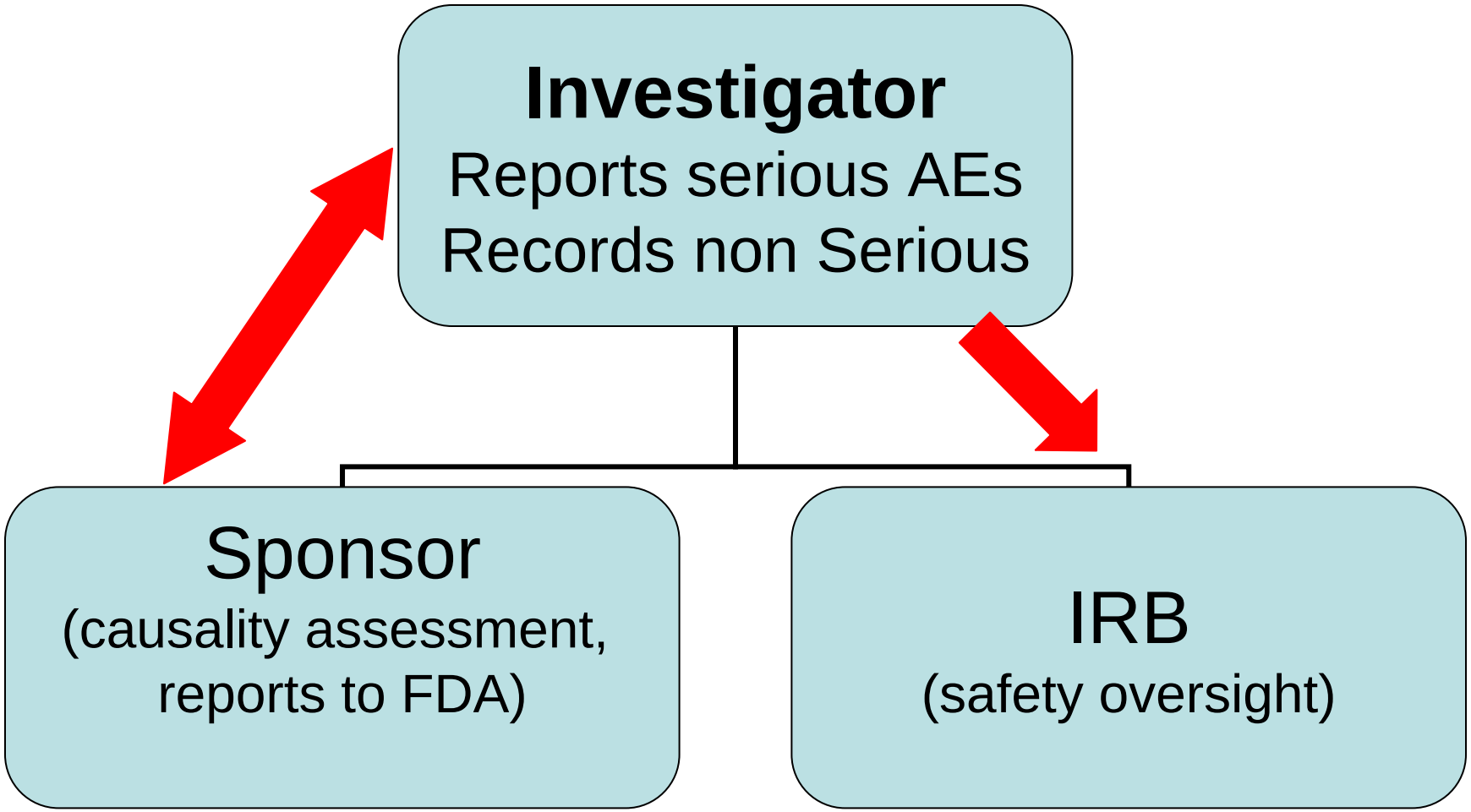
The Universe of Adverse Events



Investigator Reporting: CFR 312.64(b)

- Immediately report any serious AE to sponsor – including those listed in the Investigator Brochure or Protocol
- Investigator's assessment of causality
- Nonserious AEs are recorded and reported to the sponsor according to protocol
- Do not report study endpoints (non-acute deaths if all cause mortality is an endpoint)

Role of the Investigator



IRB Reporting CFR 312.66

- IND safety rule addresses investigator reporting to sponsor and sponsor reporting to FDA and other investigators.
- No changes in investigator IRB reporting responsibilities.
- Important IRB Reporting Requirements:

  -Providing safety reports from sponsor

  -AEs during prior med withdrawal

Special Considerations for Radiopharmaceuticals

- Single dosing & low mass dose
- Iodine allergic reactions when given for thyroid blockade prior to administration of iodine containing test imaging drug
- Maldistribution of radioactivity
- Exposure to contaminants

RDRC CFR 361.1

- Regulations have not been updated
- No mention of IRB reporting
- Experimental agents administered in doses believed to have no pharmacologic effect in humans
- Investigator responsible to report to RDRC within 7 days
- RDRC assesses causality – if related to experimental agent reports to FDA within 7 days

Background Check

- IND Safety Reporting
- http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm226358.htm

Background Check

- IRB Reporting
- http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079753.pdf
- RDRC Reporting
- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=361.1

Questions

- Thank you

Investigator Brochure

- Provides the investigator with information (clinical and nonclinical) about the investigational drug
- Used as basis for sponsor's determination if an event is "unexpected" for reporting purposes
- Content of the clinical risk information
  - Include adverse events for which a causal relationship is suspected or confirmed
- Updating the Investigator Brochure
  - Depends on strength of evidence from individual or multiple cases
  - Continue to report as unexpected until IB is updated

Outline

- Investigators: When & What to Report for:
  - IND Clinical Trials –***New*** *Rule*

Capturing Events

Reporting { Expedited / Routine

- RDRC research studies